

DEPRESSION AND DRUG NON-ADHERENCE

DR. WAJID ALI AKHUNZADA

MBBS, FCPS (Psychiatry) FACP (Psychiatry)
Assistant Professor of Psychiatry
Khyber Girls Medical College
Hayatabad Medical Complex, Peshawar

DR. RAZA UR RAHMAN

MBBS, FCPS (Psychiatry)
Assistant Professor of Psychiatry
Dow University of Health Sciences, Karachi

DR. IMTIAZ AHMAD DOGAR

MBBS, MCPS (Psychiatry) FCPS (Psychiatry)
Associate Professor & Head Department of
Psychiatry and Behavioral Sciences
Punjab Medical College, Faisalabad

Dr. Niaz Maqsood

MBBS, DPM, MCPS, FCPS
Head Department of Psychiatry
Bahawal Victoria Hospital, Bahawalpur

Article Citation:

Akhunzada WA, Dogar IA, Raza ur Rahman, Maqsood N. Depression and drug non-adherence. Professional Med J Jun 2010;17(2):340-346.

ABSTRACT... Objectives: To determine the different levels of drug non-adherence in patients suffering from Depression. **Design:** A case-controlled study. **Place and Duration of Study:** Hayatabad Medical Complex Peshawar, From February 2008 to August 2008. **Patients and Method:** 50-Cases were selected from the out patient department with the DSM-IV diagnosis of major depressive disorder, 50- non psychotic patients were selected as controls. Both sexes were included. The basic socio-demographic characteristics and the clinical profile of all the patients were collected. The level of drug non-adherence was recorded at week 4, week 8 and week 12. SPSS version 15 was used for statistical analysis. The applied method for group comparison was the Chi-square test. **Results:** The age in mean was 33.78 ± 11.30 for the sample and 30.65 ± 9.40 for control group. 38% of these patients were males and 62% females. 58% were married and uneducated from lower socio-economical class. 70% of the study group and 59% of control group received treatment. The rates of non adherence were statistically not significant at week 4. However, at week 8 and week 12 the rates of non adherence were statistically significant with the p values of less than (0.001) respectively. **Discussion:** Rates of non-adherence with psychotropic / antidepressants are difficult to summarize because they vary with setting, diagnosis, severity of illness and type of adherence difficulties. Drug non-adherence is a serious clinical problem and it has direct effects on illness management and prognosis. **Conclusions:** The available evidence suggests that the outcome for patients who vary medication doses without consulting a professional is poor.

Key words: Major depressive disorders, Antidepressants, Drug non-adherence.

INTRODUCTION

A large part of medical practice is complicated by two problems; the degree to which treatments are specific and the extent to which they are implemented (adherence problems). Depending on setting and circumstances up to half of the benefits are either nonspecific or never obtained¹.

Adherence is a major problem in the treatment of depression. Although drugs are commonly considered a critical tool in the treatment of depression, evidence from descriptive epidemiological studies confirms that about one in three patients could not complete treatment².

Adherence may be defined as the extent to which a person's behavior conforms to medical or health advice³.

The first international congress on patient counseling defined this problem as "when a patient does not follow the treatment schedule suggested to him by the physician for management of some illness, then the patient can be

Article received on: 27/03/2009
Accepted for Publication: 27/11/2009
Received after proof reading: 27/03/2010
Correspondence Address:
Dr. Wajid Ali Akhunzada
C-1 Khattak Medical Center
Dabgari Gardens Peshawar
wajidpsy@hotmail.com

patient can be described as non-compliant¹.

Errors in drug adherence may be categorized into 4-groups, errors of omission, errors of purpose (taking medicines for wrong reasons), errors of dosage and mistakes in timing or sequence⁴.

The degree to which an individual follows medical advice is a major concern in every medical specialty⁵. The extent of non-adherence in psychiatry (and perhaps its impact on the patient) may be significantly greater than in other medical specialties^{6,7}.

There are two reasons why psychiatrists need to concern themselves with the problems of adherence. The first is the implication, it has for personal practice; another is to provide expert consultation to the other health professionals on the management of adherence in general medical practice¹.

Given the necessity of therapeutic agreement the term compliance has given way to adherence and concordance⁸. In considering the nosology of concordance and adherence a useful distinction is between, the patients who do not start a medication (similarly those who do not attend their first appointment) and those who start the course but either take medication incompletely (partial adherence) or discontinue prematurely against medical advice⁸.

In Sweden Akerblad et al (2003),⁹ found that among 1031- patients with depression treated in primary care over a 6-months period only 54.6% of all scheduled appointments were kept.

The non-adherence habits of those prescribed antidepressants are recently highlighted in literature. Roughly 10% of patients prescribed antidepressants fail to pick up their first prescription and about a third collect only the initial (typically 4-weeks) prescription¹⁰. In those on long-term maintenance treatment, discontinuation rates for selective serotonin reuptake inhibitors (SSRIs), are about 70%¹¹.

Other meta-analyses, have demonstrated that for tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs), drop out rates are in the range of 21% to 33%, irrespective of the drug class^{12,13,14,15}.

Considering this enormous and complex problem of drug non-adherence, this study was designed to determine the different levels of drug non-adherence in patients suffering from depression.

PATIENTS AND METHODS

A hospital based, retrospective, case control study, with follow ups. Conducted at Hayatabad Medical Complex (HMC) Peshawar, from February 2008 to August 2008.

Fifty cases were selected from the out patients department with DSM-IV diagnosis of Major Depressive Disorder. Fifty non-psychotic patients with other psychiatric disorders were selected as control group.

Informed consent was taken from all these patients and they were interviewed the same day, using a semi structured proforma designed for this study. Both sexes were included.

The basic sociodemographic characteristics and the clinical profile of all the patients were collected. The level of drug non-adherence was recorded at week 4, week 8 and week 12. SPSS version 15 was used for statistical analysis.

RESULTS

The mean age of study group was 33.78 ± 11.3 years as compared to 30.65 ± 9.40 years of control group. 62% of the participants were women. Majority of the participants were married, house-wives, from the lower socio-economic class and rural area of living. There were no significant differences in the socio-demographic characteristics between the two groups. The socio-demographic characteristics of study sample and controls are summarized in table-I.

Table-II shows the clinical profile of all the patients. The clinical profile indicated that the illness onset was acute,

with predominantly short duration of illness. 70% of the sample and 59% of the control group received treatment within 1.50 months and 1.55 months respectively. 38% of the study group as compared to 22% of the control group never had any relapses.

Table-III, shows the different levels of drug non-adherence. The rates of non adherence at week-4 were statistically not significant, with the P-value of (0.003) Which were higher than the predetermined statistically significant P- Value of (0.001). However, at week 8 and week 12 the rates of non adherence were statistically significant with the P-values of less than (0.001) respectively.

DISCUSSION

In the present study the most affected age group was from 25-35years with a mean of 33.78 ± 11.30 , which is also reported in national^{16,17} and international studies^{18,19,20} 38% of our study group were men and 62% women, which is a common and most consistent finding reported in the international literature^{21,22,23}, on depression with the ratio of 1:1.9 of men to women.

Boyed and Weisman,²⁴ found depression, to be more frequent in divorced and separated, while up to 58% of our sample were married. Similar results are reported by Chaudhri et al in local study¹⁷.

National^{16,17} and international studies¹⁹ have reported increased frequency of depression in the lower socio-economical groups. 68% of our sample had acute onset, 70% of them already received treatment with an antidepressant drug and 38% had no relapses of depression.

The present study was conducted to determine the different levels of drug adherence, with antidepressants drugs, as compared to the drug adherence of a non-psychotic, control group. This comparison was done with a follow-up designed at week-4, week -8 and week 12.

The rates of non adherence were statistically not significant with a P-value of (0.003) at week 4. While, we

Table-I. Socio-demographic characteristics of study sample and controls.		
Variable	Sample (%) n=50	Control (%) n=50
Age (mean)	33.78±11.30*	30.65±9.40*
Sex		
Males	38%	38%
Females	62%	62%
Marital status		
Single	30%	33%
Married	58%	57%
Widowed	9%	7%
Separated	3%	3%
Education		
Uneducated	46%	48%
Primary	22%	25%
Middle	12%	10%
Secondary	10%	9%
Intermediate	6%	5%
Graduation	3%	2%
Post graduation	1%	1%
Employment		
Govt-employed	8%	6%
Self employed	12%	14%
Un-employed	28%	26%
Student	10%	6%
House wife	42%	48%
Socio-economical status		
Upper	2%	1%
Middle	21%	15%
Lower	77%	84%
Area of living		
Urban	46%	40%
Rural	54%	60%

Table-II. Clinical characteristics of study sample and controls.

Variable	Sample (%) n=50	Control (%) n=50
Onset of illness		
Acute	68%	64%
Insidious	32%	36%
Duration of illness		
1 month	34	31
1 to 6 month	14	15
2 to 6 months	21	23
6 months to 1 year	17	19
More than 1 year	14	12
First contact for treatment (in months)	1.50±0.50*	1.55±0.52*
Past history of psychiatric illness		
Present	33%	39%
Absent	67%	61%
Family history/psychiatric illness		
Present	46%	41%
Absent	54%	59%
Treatment status		
Received treatment	70%	59%
Partially treated	12%	24%
Un-treated	18%	17%
Relapses		
No relapse	38%	22%
One relapse	16%	30%
Two relapses	17%	21%
Three relapses	15%	18%
More than 4 relapses	14%	9%

noted a statistically significant difference, in the level of drug non-adherence, between the study sample and the control group, at week-8 and week-12 with the P-values of (0.001) respectively.

In a study of 200 patients attending 14- family physicians in five different practices, Johnson in 1981,²⁵ found that the drug non adherence rates were 16% at week 1, 41% at week two, 59% at week three and 68% at week four.

Generally the rates of non-adherence with psychotropic / antidepressants are difficult to summarize because they vary by setting, diagnosis, severity of illness and type of adherence difficulties.

Drug non-adherence is a serious clinical problem and it has direct effects on illness management and prognosis²⁶. Early non-adherence increases the risk of further non –attendance. Socio-economic factors and degree of social supervision may also influence a patient's drug adherence.

The available evidence suggest that the outcome for patients who vary medication doses without consulting a professional is poorer^{27,28}. For this very reason, poor drug non-adherence, the long term out-come of depression remains relatively poor, remission often followed by continuing residual symptoms, early relapse and latter recurrence^{29,30,31,32}.

The present study was conducted to determine the different levels of drug non-adherence and it was not meant to find out the different causes, reasons and factors leading to problems of drug- non adherence.

CONCLUSIONS

The combination of psycho-educational approaches, like compliance therapy³³ with adequate and effective psycho-pharmacotherapy and appropriate education of the family members regarding depression and its course and prognosis, along with rehabilitation, are the best means of improving drug adherence and hence recovery from severe depression.

Table-III. Non-adherence at week 4, week 8 and week 12.					
Drug adherence in different groups at week 4					
	Drug adherence in the last month				P-value
	90% of the time	50-90% of the time	10-50% of the time	less than 10% of the time	
case	14(24.6%)	25(78.1%)	8(100.0%)	3(100.0%)	0.003
control	43(75.4%)	7(21.9%)	0(0.0%)	0(0.0%)	
Drug adherence in different groups at week 8					
	Drug adherence in the last month				P-value
	90% of the time	50-90% of the time	10-50% of the time	less than 10% of the time	
case	8(21.1%)	21(55.3%)	20(90.9%)	1(50.0%)	<0.001
control	30(78.9%)	17(44.7%)	2(9.1%)	1(50.0%)	
Drug adherence in different groups at week 12					
	Drug adherence in the last month				P-value
	90% of the time	50-90% of the time	10-50% of the time	less than 10% of the time	
case	3(10.7%)	12(33.3%)	32(97.0%)	3(100.0%)	<0.001
control	25(89.3%)	24(66.7%)	1(3.0%)	0(0.0%)	

Therefore, clinicians need to examine their own roles in the formation of the therapeutic alliance, including their attitudes, their ability to listen and respond to the patient's concerns (and beliefs about medication), and the quality and quantity of information they give, to the patients and their family members.

CLINICAL IMPLICATIONS

Given the high risk of missed medication and missed appointments in psychiatry it is suggested that methods are developed that help patients who have adherence or attendance difficulties.

These methods should be applicable to the routine clinical care and most effective in our setting.

Copyright© 27 Nov, 2009.

REFERENCES

1. Barry Black; **Treatment Adherence** – British Journal of Psychiatry 1976;129,513-31.
2. Pampallona, S, Bollini P, Tibalsdi G, et al. **Patient adherence in the treatment of depression**. British Journal of Psychiatry 2002;180,104-109.
3. Bruer, J. T. **Methodological rigors and citation frequency in patient compliance literature**. American Journal of public health, 1982;72.1119-1123.
4. Malahy, B. **The Effects of Instructions and Labeling on the number of medication errors made by patients at home**. American Journal of Hospital Pharmacology 1966;23:283-92.
5. Osterberg ,L & Blaschke, T. **Adherence to medication**. New England Journal of Medicine 2005;353,487-497.
6. Mitchell, A. J. & Selmes, T. Why don't patients take their medicine? **Reasons and solutions in Psychiatry**. Advances I Psychiatric Treatments 2007;Vol.13,336-346.
7. Ali, W, Rehman, W & Maqsood, N. **Schizophrenia and Drug Non- Compliance**. The Professional Medical Journal, 2006;Vol:13, No:03, July, August, September. 423-430.

8. Haynes, R. McDonald, H & Garg, A. **Interventions for helping patients to follow prescriptions for medication. Cochrane Database of Systematic reviews, Issue 2.** Update software 2002.
9. Akerblad, A C, Bengtsson, F, Ekselius, L, et al. **Effects of an educational compliance enhancement programme and therapeutic drug monitoring on treatment adherence in depressed patients managed by general practitioners.** International Clinical Psychopharmacology, 2003;18,347-354.
10. Bultman, D. C & Svarstad, B. L. **Effects of pharmacist monitoring on patient's satisfaction with antidepressant medication therapy.** Journal of the American Pharmaceutical Association, 2002;42,36-43.
11. Mullins, C. D, Shaya, F. T, Meng, F, et al. **Persistence, switching and discontinuation rates among patients receiving sertraline, paroxetine and citalopram.** Pharmacotherapy, 2005;25,660-667.
12. Anderson, I. M. & Tomenson, B. M. **Discontinuation with selective serotonin reuptake inhibitors compared with tricyclic antidepressants: a meta-analysis.** British Medical Journal, 1995;310,1433-1438.
13. Montgomery, S. A. & Kasper, S. **Comparison of compliance between serotonin reuptake inhibitors and tricyclic antidepressants: a meta-analysis.** International Clinical Psychopharmacology, 1995;9,33-40.
14. Steffens, D. C, Krishnan, K. R & Helms, M. J. **Are SSRIs better than TCAs ? Comparison of SSRIs and TCAs: a meta-analysis.** Depression and Anxiety. 1997;6,10-18.
15. Anderson, I. M. **SSRIs versus tricyclic antidepressants in depressed patients: a meta-analysis of efficacy and tolerability.** Depression and Anxiety.7 (suppl.1), 1998;11-17.
16. Ali, W. Ali. **Socio-Demographic study of Depression. Journal of Medical Sciences.** Vol. 9, No; 1, March 1999; 24-30.
17. Chaudhri M. A, Ahmad. M ,Jehangir. S. **Patterns of somatization in depression.** Pakistan Armed Forces Medical Journal,1994,44(1);89-91.
18. Coryell. W. Endocott. J.E., Keller. M. **Major depression in a non-clinical sample, demographic and clinical risk factors for first onset.** Archive of general psychiatry. 1992;49:117-125.
19. Pakel E.S. Basoglu, M. Ulusahin A. **A cross-cultural comparative study of depressive symptoms in British and Turkish clinical samples.** Social psychiatry psychiatric epidemiology.1994;29:31-39.
20. Robins N, Helzer J. E, Weissman. M. M, et al. **Life time prevalence of specific psychiatric disorders, in three sites.** Archive of General Psychiatry; 1984;41:949-958.
21. Piccinelli M, Wilkinson G. **Gender and Depression.** British Journal of Psychiatry. 2000;177:486-492.
22. Briscoe M. E, Barouero J. L. V, William P, Manrioue J. P, Pena C. **Sex differences in the differentiation of psychiatric symptomatology.** British Journal of Psychiatry, 1989;154:364-367.
23. Weissman. M. M, Klerman. G. **Gender and depression.** Trends in Neurosciences, 8, 416-420. Harris T. **Is sex necessarily a risk factor to depression?** British Journal of Psychiatry 1985 (1991) 1589,708-712.
24. Boyd J. H, Weissman. M. M. **Epidemiology hand book of affective disorders.** Edinbergh. Churchill Livingstone 1982.
25. Johnson, D. A. **Depression Treatment compliance in general practice.** Acta Psychiatrica Scandinavica Supplementum, 1981;290,447-453.
26. Taj, R. Khan. S & Khan A, et. **Non-Compliance to treatment in schizophrenic patients.** Journal of Pakistan Psychiatric Society, 2003;Vol.1(1).27-29.
27. Carpenter, P. J, Morrow, G. R., Del, Gauio, A.C, et al. **Who Keeps the first outpatient appointment?** American Journal of Psychiatry, 1981;138;102-105.
28. Svarstad , B. I, Shireman, T & Sweeny, J. **Using drug claims data to assess the relationship of medication adherence with hospitalization and costs.** Psychiatrica Service,2001;52:8085-811.
29. Keller, M. B, Mueller, T. I, et al. **Time to recovery, chronicity, and levels of psychopathology in major depression.** Archives of General Psychiatry,1992;49:809-816.
30. Mueller, T. I, Keller. M. B., Leon, A. C, et al. **Recovery after 5 years of unremitting major depressive disorder.** Archive of General Psychiatry, 1996;53:794-799.

31. Paykel, E. S, Ramana, R, Cooper, Z, et al. **Residual symptoms after partial remission: an important outcome in depression.** Psychological Medicine, 1995; 25:1171-1180.
32. Ramana, R, Paykel, E. S, Cooper, Z, et al. **Remission and relapse in major depression a two year prospective follow-up study.** Psychological Medicine, 1995;25:1161-1170.
33. Kemp. R, Kirov. G, Everitt. B, Hayward. P and David A. **Randomized controlled trial of compliance therapy.** 18-months follow-up. British Journal of Psychiatry, 1998; 172:413-419.

The advertisement features a blue-toned image of a fountain pen nib pointing towards the bottom left. The background is a collage of Arabic calligraphy and a globe icon. The text 'H-2000' is visible near the pen nib. Below the pen, the text 'INDEPENDENT REVIEWS' is written in large, bold, white capital letters. Underneath that, the slogan 'A soul mate in writing' is displayed. A small box on the left indicates 'Vol: 12, No. 1-3' and '2010 Jan, Feb, Mar'. At the bottom, the website 'www.indepreview.com' is listed.